# Dynamics of a Networked Connectivity Model of Waterborne Disease Epidemics 

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- Background on waterborne diseases
- Introduction to epidemic model and parameters
- Local stability analysis
- Lyapunov functions and global stability analysis
- Bifurcation analysis
- (Non)Existence of periodic solutions
- Our contribution


## Waterborne Diseases

- Mainly caused by protozoa or bacteria present in water.
- Waterborne diseases are one of the leading causes of death in low-income countries, particularly affecting infants and children in those areas.
- The models we have been studying use mainly V . cholera as an example.
- Vast majority of models in the literature consider one single community.
- First networked connectivity model introduced in late 2012.


## Why Are We Studying This Model?

- Learn about dynamical systems
- To gain a better understanding of:
- Onset conditions for outbreak
- The spread of diseases by hydrological means
- Insight
- Emergency management
- New health-care resources


## Reproduction Matrices/Values

- $R_{0}$ is known as the basic reproduction number in SIR and related models.
- This stands only when $n=1$ (most research articles study only this case)
- Outbreak occurs when $R_{0}>1$
- With networked connectivity, this statement does not hold.
- For connectivity models, we study $G_{0}$, or the generalized reproduction matrix. When the dominant eigenvalue of this matrix crosses the value one, an outbreak will occur. This value is independent from the values of $R_{0 i}$.


## Bifurcations

- Bifurcation occurs when small changes in parameters imply drastic changes in the solutions, number of equilibrium points, or their stability properties.
- Disease-free equilibrium
- Transcritical Bifurcation


## The Model

Consider $n$ communities (nodes). For $i=1, \ldots, n$, let

- $S_{i}=$ number of susceptibles in node $i$
- $I_{i}=$ number of infectives in node $i$
- $B_{i}=$ concentration of bacteria in water at node $i$
- Spatially explicit nonlinear differential model
- Communities are connected by hydrological and human mobility networks through which a disease can spread.


## Strongly Connected



Graph $\Gamma(\mathbf{P} \cup \mathbf{Q})$ is strongly connected.

## The Epidemic Model (Gatto et al.)

For $i=1, \ldots, n \quad$ (3n differential equations)

$$
\begin{aligned}
\frac{d S_{i}}{d t} & =\mu\left(H_{i}-S_{i}\right)-\left[\left(1-m_{s}\right) \beta_{i} f\left(B_{i}\right)+m_{s} \sum_{j=1}^{n} Q_{i j} \beta_{j} f\left(B_{j}\right)\right] S_{i} \\
\frac{d l_{i}}{d t} & =\left[\left(1-m_{s}\right) \beta_{i} f\left(B_{i}\right)+m_{s} \sum_{j=1}^{n} Q_{i j} \beta_{j} f\left(B_{j}\right)\right] S_{i}-\phi I_{i} \\
\frac{d B_{i}}{d t} & =-\mu_{B} B_{i}+I\left(\sum_{j=1}^{n} P_{j i} \frac{W_{j}}{W_{i}} B_{j}-B_{i}\right)+\frac{p_{i}}{W_{i}}\left[\left(1-m_{l}\right) l_{i}+\sum_{j=1}^{n} m_{l} Q_{j i} I_{j}\right]
\end{aligned}
$$

where $f\left(B_{i}\right)=\frac{B_{i}}{K+B_{i}}$.

## (Local)Stability Analysis of a Single Community

For $n=1$, the model is

$$
\begin{aligned}
\frac{d S}{d t} & =\mu(H-S)-\beta f(B) S \\
\frac{d l}{d t} & =\beta f(B) S-\phi I \\
\frac{d B}{d t} & =(n b-m b) B+p l
\end{aligned}
$$

where $f(B)=\frac{B}{K+B}$.

## Linearization

## Definition

A set $S \subset R^{n}$ is said to be invariant with respect to $x^{\prime}=f(x)$ if $x(0) \in S \Longrightarrow x(t) \in S$ for all $t \geq 0$.

## Linearization Technique:

Consider the nonlinear system $x^{\prime}=f(x) \quad$ in $R^{n}$
Let $x_{0}$ be a hyperbolic equilibrium point $\left(f\left(x_{0}\right)=0\right)$
Local stability analysis: Study the linear system $\quad x^{\prime}=A x$, where

$$
A=\operatorname{Df}\left(x_{0}\right), \quad \operatorname{Df}(x)=\left[\begin{array}{ccc}
\frac{\partial f_{1}}{\partial x_{1}} & \cdots & \frac{\partial f_{1}}{\partial x_{n}} \\
\vdots & & \vdots \\
\frac{\partial f_{n}}{\partial x_{1}} & \cdots & \frac{\partial f_{n}}{\partial x_{n}}
\end{array}\right]
$$

## (Local)Stability Analysis of a Single Community

## Theorem

Stable Manifold Theorem: Let $E$ be an open subset of $R^{n}$ containing the equilibrium point $x_{0}$ of $x^{\prime}=f(x)$, and let $f \in C^{1}(E)$. Suppose that $D f\left(x_{0}\right)$ has $k$ eigenvalues with negative real part and $n-k$ eigenvalues with positive real part. Then there exists a $k$-dimensional differentiable manifold $\mathbf{S}$ tangent to the stable subspace $E^{s}$ of the linear system $x^{\prime}=\mathbf{A} x$ at $x_{0}$ such that $\mathbf{S}$ is invariant, and solutions approach $x_{0}$ as $t \rightarrow \infty$. And there exists an $n-k$ dimensional differentiable manifold $\mathbf{U}$ tangent to the unstable subspace $E^{u}$ of $x^{\prime}=\mathbf{A} x$ at $x_{0}$ such that $\mathbf{U}$ is invariant and solutions move away from $x_{0}$ as $t \rightarrow \infty$.

## Theorem

Hartman - Grobman Theorem: Let $E$ be and open subset of $R^{n}$ containing a hyperbolic equilibrium point $x_{0}$ of $x^{\prime}=f(x)$, and let $f \in C^{1}(E)$. Then there exists a homeomorphism $\mathbf{H}$ of an open set $U$ containing $x_{0}$ into an open set $V$ containing $x_{0}$ such that $H$ maps trajectories of $x^{\prime}=f(x)$ near $x_{0}$ onto the trajectories of $x^{\prime}=\mathbf{A} x$ near $x_{0}$.

## (Local)Stability Analysis of a Single Community




## (Local)Stability Analysis of a Single Community

For this model, the general Jacobian is

$$
J(S, I, B)=\left[\begin{array}{ccc}
-\mu-\frac{\beta B}{K+B} & 0 & -\frac{\beta S K}{(K+B)^{2}} \\
\frac{\beta B}{K+B} & -\phi & \frac{\beta S K}{(K+B)^{2}} \\
0 & p & n b-m b
\end{array}\right]
$$

## Disease-Free Equilibrium

$$
S_{1}^{*}=H, I_{1}^{*}=0, B_{1}^{*}=0
$$

$$
A=\mathbf{J}\left(S_{1}^{*}, l_{1}^{*}, B_{1}^{*}\right)=\left[\begin{array}{ccc}
-\mu & 0 & -\frac{\beta H}{K} \\
0 & -\phi & \frac{\beta H}{K} \\
0 & p & n b-m b
\end{array}\right]
$$

Characteristic Equation:

$$
\begin{aligned}
P(\lambda)= & \lambda^{3}+(\mu+\phi-n b+m b) \lambda^{2}+ \\
& +\left(\mu \phi+(\mu+\phi)(m b-n b)-\frac{\beta H p}{K}\right) \lambda+ \\
& +\mu \phi m b-\mu \phi n b-\frac{\mu \beta H p}{K}
\end{aligned}
$$

## Routh-Hurwitz Criteria

## Theorem (Routh-Hurwitz)

Given the polynomial,

$$
P(\lambda)=\lambda^{n}+a_{1} \lambda^{n-1}+\ldots+a_{n-1} \lambda+a_{n}
$$

where the coefficients $a_{i}$ are real constants, $i=1, \ldots, n$. For polynomials of degree $n=3$, the Routh-Hurwitz criteria are summarized by

$$
a_{1}>0, a_{3}>0, \quad \text { and } a_{1} a_{2}>a_{3} .
$$

These are necessary and sufficient conditions for all of the roots of the characteristic polynomial (with real coefficients) to lie in the left half of the complex plane (implying stability).

## Disease-Free Equilibrium

By applying the Routh - Hurwitz Criteria to the characteristic equation, it was found that $a_{1}>0, a_{3}>0$, and $a_{1} a_{2}>a_{3}$, were true for the following inequalities,

$$
m b>n b, \quad S_{c}=\frac{\phi K(m b-n b)}{\beta p}>H=S_{0} .
$$

Let $R_{0}=\frac{S_{0}}{S_{c}}$, then $R_{0}<1$ and our equilibrium is stable.

## Basic Reproduction Number $R_{0}$

In the previous model, $R_{0}=\frac{\beta p S_{0}}{\phi K(m b-n b)}=\frac{S_{0}}{S_{c}}$. How is $R_{0}$ determined in general?

## Theorem (Castillo-Chavez et al.)

Consider the $\left(n_{1}+n_{2}+n_{3}\right)$-dimensional system

$$
\begin{aligned}
x^{\prime} & =f(x, E, I) \\
E^{\prime} & =g(x, E, I) \\
I^{\prime} & =h(x, E, I)
\end{aligned}
$$

Let $\left(x^{*}, 0,0\right)$ be the disease-free equilibrium. Assume the equation $g\left(x^{*}, E, I\right)=0$ implicitly determines a function $E=\tilde{g}\left(x^{*}, I\right)$, and let $A=D_{l} h\left(x^{*}, \tilde{g}\left(x^{*}, 0\right), 0\right)$. Assume further that $A$ can be written as $A=M-D$, where $M \geq 0$ and $D>0$ is diagonal. Then,

$$
R_{0}=\rho\left(M D^{-1}\right)
$$

## Lyapunov Functions and Global Stability

## Definition

Let $E$ be an open set in $R^{n}$, and let $x_{0} \in E$. A function $Q: E \subset R^{n} \rightarrow R$ is called a Lyapunov function for $x^{\prime}=f(x)$ if $Q \in C^{1}(E)$ and satisfies $Q\left(x_{0}\right)=0$, and $Q(x)>0$ if $x \neq x_{0}$.

## Theorem

Let $R_{0} \leq 1, m b>n b$, and let $\mathbf{w}$ be a left eigenvector of the matrix $\mathbf{V}^{-1} \mathbf{F}$ corresponding to $R_{0}=\rho\left(\mathbf{V}^{-1} \mathbf{F}\right)$, then the function $Q(\mathbf{x})=\mathbf{w}^{T} \mathbf{V}^{-1} \mathbf{x}$ is a Lyapunov function of the system of equations for $n=1$ satisfying $Q^{\prime}(\mathbf{x}(t)) \leq 0$.

## Lyapunov Functions and Global Stability

Our system can be written as compartmental model

$$
\mathbf{x}^{\prime}=\mathbf{F}^{*}(x, y)-\mathbf{V}^{*}(x, y), \quad y^{\prime}=g(x, y)
$$

where $x=[I, B]^{T} \in R^{2}$ is the disease compartment and $y=S \in R$ is the disease-free compartment, respectively. And

$$
\mathbf{F}=\left[\frac{\partial F_{i}^{*}}{\partial x_{j}}\left(0, y_{0}\right)\right] \quad \text { and } \quad \mathbf{V}=\left[\frac{\partial V_{i}^{*}}{\partial x_{j}}\left(0, y_{0}\right)\right], \quad 1 \leq i, j \leq n
$$

## Lyapunov Functions and Global Stability

Let $\mathbf{F}^{*}=\left[\begin{array}{ll}\frac{\beta S B}{K+B} & p \prime\end{array}\right]^{T}$ and $\mathbf{V}^{*}=\left[\begin{array}{ll}-\phi l & (m b-n b) B\end{array}\right]^{T}$, then the matrices $\mathbf{F}$ and $\mathbf{V}$ are given by

$$
\mathbf{F}=\left[\begin{array}{cc}
0 & \frac{B H}{K} \\
p & 0
\end{array}\right], \quad \mathbf{V}=\left[\begin{array}{cc}
\phi & 0 \\
0 & m b-n b
\end{array}\right] .
$$

The matrix

$$
\mathbf{V}^{-1} \mathbf{F}=\left[\begin{array}{cc}
0 & \frac{\beta H}{K \phi} \\
\frac{p}{m b-n b} & 0
\end{array}\right]
$$

leads us to

$$
\rho\left(\mathbf{V}^{-1} \mathbf{F}\right)=R_{0}=\sqrt{\frac{\beta H p}{K \phi(m b-n b)}}
$$

## Lyapunov Functions and Global Stability

The left eigenvector is found to be $\mathbf{w}^{T}=\left[\begin{array}{ll}1 & R_{0}\left(\frac{m b-n b}{p}\right)\end{array}\right]$. As $Q(\mathbf{x})=\mathbf{w}^{T} \mathbf{V}^{-1} \mathbf{x}$, we can now write it as

$$
Q=\left[\begin{array}{ll}
1 & R_{0}\left(\frac{m b-n b}{p}\right)
\end{array}\right]\left[\begin{array}{cc}
\frac{1}{\phi} & 0 \\
0 & \frac{1}{m b-n b}
\end{array}\right]\left[\begin{array}{l}
l \\
B
\end{array}\right]=\frac{l}{\phi}+\frac{R_{0} B}{p} .
$$

Now let $\mathbf{f}(x, y)=(\mathbf{F}-\mathbf{V}) x-\mathbf{x}^{\prime}$ and $Q^{\prime}=\mathbf{w}^{\top} \mathbf{V}^{-1} \mathbf{x}^{\prime}=\left(R_{0}-1\right) \mathbf{w}^{T} \mathbf{x}-\mathbf{w}^{T} \mathbf{V}^{-1} \mathbf{f}(x, y)$, where

$$
f(x, y)=\left[\begin{array}{c}
\frac{\beta H B}{k}-\frac{\beta S B}{K+B} \\
0
\end{array}\right]
$$

$Q^{\prime}=\left(R_{0}-1\right)\left(I+\frac{R_{0} B}{p}(m b-n b)\right)-\frac{\beta B}{\phi}\left(\frac{H}{K}-\frac{S}{K+B}\right) \leq 0$.

## Lyapunov Functions and Global Stability

## Theorem (LaSalle's Invariance Principle)

Let $\Omega \subset D \subset R^{n}$ be a compact invariant set with respect to $x^{\prime}=f(x)$. Let
$Q: D \rightarrow R$ be a $C^{1}$ function such that $Q^{\prime}(x(t)) \leq 0$ in $\Omega$. Let $E \subset \Omega$ be the set of all points in $\Omega$ where $Q^{\prime}(x)=0$. Let $M \subset E$ be the largest invariant set in $E$. Then

$$
\lim _{t \rightarrow \infty}\left[\inf _{y \in M}\|x(t)-y\|\right]=0
$$

That is, every solution starting in $\Omega$ approaches $M$ as $t \rightarrow \infty$.

## Theorem

Let $\Omega$ be any compact invariant set containing the disease-free equilibrium point. Let $\mathbf{f}, \mathbf{F}$, and $\mathbf{V}$ be defined as above. Suppose $R_{0}<1$, $m b>n b$, and $\mathbf{f}(x, y) \geq 0, \mathbf{F} \geq 0, \mathbf{V}^{-1} \geq 0, \mathbf{f}(0, y)=0$. Also, assume the disease-free system $y^{\prime}=g(0, y)$ has a unique equilibrium $y=y_{0}>0$ that is globally asymptotically stable in $R$. Then, the disease-free equilibrium is globally asymptotically stable in $\Omega$.

## Lyapunov Functions and Global Stability

The disease-free system $y^{\prime}=g(0, y)$ is equivalent to $S^{\prime}=\mu H-\mu S$, whose solution is $S=H+e^{-\mu t} C$.
$y_{0}=H$ is globally asymptotically stable in the disease-free system.
$Q^{\prime}=\left(R_{0}-1\right) \mathbf{w}^{T} \mathbf{x}-\mathbf{w}^{T} \mathbf{V}^{-1} \mathbf{f}(x, y)$. Assuming $Q^{\prime}=0$ implies $\mathbf{x}=0$. Then, the set of all points where $Q^{\prime}=0$ is $E=\{(I, B, S): I=B=0\}$. The largest and only invariant set in $E$ is $(0,0, H)$.

Therefore, the disease-free equilibrium is globally asymptotically stable in $\Omega$.

## Endemic Equilibrium

The endemic equilibrium represents a single isolated community where there is interaction between susceptibles, infectives, and bacteria in water.

$$
\begin{aligned}
S_{2}^{*} & =\frac{\mu H(K+B)}{\mu(K+B)+\beta B} \\
I_{2}^{*} & =\frac{\beta B \mu H}{\phi(\mu(K+B)+\beta B)} \\
B_{2}^{*} & =\frac{\mu(p \beta H+K \phi(n b-m b))}{\phi(\mu+\beta)(m b-n b)}
\end{aligned}
$$

## Endemic Equilibrium

$$
\text { Let } \begin{aligned}
A=\frac{\beta B}{K+B} \text { and } C & =\frac{\beta S K}{(K+B)^{2}}, \\
\mathbf{J}\left(S_{2}^{*}, I_{2}^{*}, B_{2}^{*}\right) & =\left[\begin{array}{ccc}
-(\mu+A) & 0 & -C \\
A & -\phi & C \\
0 & p & n b-m b
\end{array}\right]
\end{aligned}
$$

Using Routh-Hurwitz criteria: As long as $H>S_{c}$ (or $R_{0}>1$ ), all real parts of the eigenvalues are negative, making the endemic equilibrium locally stable.

Therefore, endemic equilibrium is stable exactly when disease-free equilibrium is unstable.

## Phase Portrait

$\beta=1, \phi=0.2, \mu=0.0001, p=10, m b=0.4, n b=0.067, H=$ $10000, K=1000000$ and $S_{c}=6660$


## Bifurcations

## Theorem (Sotomayor)

Consider $x^{\prime}=\mathbf{f}(\mathbf{x}, \alpha)$, where $\mathbf{x} \in R^{n}$ and $\alpha$ is a parameter. Let ( $\mathbf{x}_{0}, \alpha_{0}$ ) be an equilibrium point and assume $\mathbf{A}=D \mathbf{f}\left(\mathbf{x}_{0}, \alpha_{0}\right)$ has a simple eigenvalue $\lambda=0$ with eigenvector $\mathbf{v}$, and left eigenvector $\mathbf{w}$. If
$\mathbf{w}^{T} \mathbf{f}_{\alpha}\left(x_{0}, \alpha_{0}\right)=0$,
$\mathbf{w}^{T}\left[D \mathbf{f}_{\alpha}\left(\mathbf{x}_{0}, \boldsymbol{\alpha}_{0}\right) \mathbf{v}\right] \neq 0$,
$\mathbf{w}^{T}\left[D^{2} \mathbf{f}\left(\mathbf{x}_{0}, \boldsymbol{\alpha}_{0}\right)(\mathbf{v}, \mathbf{v})\right] \neq 0$
then a transcritical bifurcation occurs at $\left(\mathrm{x}_{0}, \boldsymbol{\alpha}_{0}\right)$.
Note: $D^{2} \mathbf{f}\left(\mathbf{x}_{0}\right)(\mathbf{u}, \mathbf{v})=\sum_{j_{1}=1}^{n} \sum_{j_{2}=1}^{n} \frac{\partial^{2} \mathbf{f}\left(\mathbf{x}_{0}\right)}{\partial x_{j_{1}} \partial x_{j_{2}}} u_{j_{1}} v_{j_{2}}$

## Bifurcations

## Theorem

The $n=1$ system undergoes a transcritical bifurcation at the disease-free equilibrium point $\left(S_{1}^{*}, l_{1}^{*}, B_{1}^{*}\right)=(H, 0,0)$ when $p=\frac{\phi(m b-n b) K}{\beta H}$, and $m b>n b$.

## Proof:

Stability of the system at the equilibrium point depends on the bottom right $2 \times 2$ matrix of $\mathbf{J}$, given by

$$
\mathbf{J}=\left[\begin{array}{ccc}
-\mu & 0 & -\frac{\beta H}{K} \\
0 & -\phi & \frac{\beta H}{K} \\
0 & p & n b-m b
\end{array}\right] \quad \mathbf{J}^{*}=\left[\begin{array}{cc}
-\phi & \frac{\beta H}{K} \\
p & n b-m b
\end{array}\right] .
$$

When the $\operatorname{det}^{*}=0, p=p_{0}=\frac{\phi(m b-n b) K}{\beta H}$.

## Sotomayor's Theorem

To satisfy the first condition of the theorem, $\mathbf{w}^{\top} \mathbf{f}_{p}\left(\mathbf{x}_{0}, p_{0}\right)=0$, we have $\mathbf{w}^{T}=\left[\begin{array}{lll}0 & 1 & \frac{\phi}{p}\end{array}\right]$, and $\mathbf{f}_{p}=\left[\begin{array}{l}0 \\ 0 \\ l\end{array}\right]$. Then,

$$
\mathbf{w}^{T} \mathbf{f}_{p}\left(\mathbf{x}_{0}, p_{0}\right)=\left[\begin{array}{lll}
0 & 1 & \frac{\phi}{p}
\end{array}\right]\left[\begin{array}{l}
0 \\
0 \\
0
\end{array}\right]=0
$$

## Sotomayor's Theorem

To satisfy the second condition of the theorem,

$$
\mathbf{w}^{T}\left[D \mathbf{f}_{p}\left(\mathbf{x}_{0}, \mathbf{p}_{0}\right) \mathbf{v}\right] \neq 0 \text {, we have } D \mathbf{f}_{p}=\left[\begin{array}{ccc}
0 & 0 & 0 \\
0 & 0 & 0 \\
0 & 1 & 0
\end{array}\right] \text {. Then }
$$

$$
\mathbf{w}^{T}\left[D \mathbf{f}_{p}\left(\mathbf{x}_{0}, p_{0}\right) \mathbf{v}\right]=\left[\begin{array}{lll}
0 & 1 & \frac{\phi}{p}
\end{array}\right]\left(\left[\begin{array}{ccc}
0 & 0 & 0 \\
0 & 0 & 0 \\
0 & 1 & 0
\end{array}\right]\left[\begin{array}{c}
\frac{-\beta H}{K \mu} \\
\frac{m b-n b}{p} \\
1
\end{array}\right]\right)
$$

$$
=\frac{\phi(n b-m b)}{p^{2}} \neq 0 .
$$

## Sotomayor's Theorem

To satisfy the third condition of the theorem, $\mathbf{w}^{T}\left[D^{2} \mathbf{f}\left(\mathbf{x}_{0}, \mathbf{p}_{0}\right)(\mathbf{v}, \mathbf{v})\right] \neq 0$, we have

$$
\begin{aligned}
& D^{2} \mathbf{f}\left(\mathbf{x}_{0}, p_{0}\right)(\mathbf{v}, \mathbf{v})=\left[\begin{array}{c}
\frac{2 \beta H}{K^{2}}\left(\frac{\beta}{\mu}+1\right) \\
-\frac{2 \beta H}{K^{2}}\left(\frac{\beta}{\mu}+1\right) \\
0
\end{array}\right] \text {. Then } \\
& \mathbf{w}^{\top}\left[D^{2} \mathbf{f}\left(\mathbf{x}_{0}, p_{0}\right)(\mathbf{v}, \mathbf{v})\right]=\left[\begin{array}{ll}
0 & 1 \\
\frac{\phi}{p}
\end{array}\right]\left[\begin{array}{c}
\frac{2 \beta H}{K^{2}}\left(\frac{\beta}{\mu}+1\right) \\
-\frac{2 \beta H}{K^{2}}\left(\frac{\beta}{\mu}+1\right) \\
0
\end{array}\right] \\
&=-\frac{2 \beta H}{K^{2}}\left(\frac{\beta}{\mu}+1\right) \neq 0 .
\end{aligned}
$$

## Bifurcations

Figure ：$p<p_{0}$


## Bifurcations

Figure ：$p=p_{0}$


## Bifurcations

Figure ：$p>p_{0}$


## Hopf Bifurcation

A stable focus (solutions spiral toward the equilibrium) corresponds to $\lambda=a \pm b i$ where $a<0$. When $a=0$, stability may be lost, periodic orbits may appear, and a Hopf Bifurcation could occur. The main the condition to prove the existence of a Hopf Bifurcation is $\lambda= \pm b i$.

Proposition: A Hopf Bifurcation at the DFE does not exist.

## Proof.

For the lower right block of Jacobian at the equilibrium, we have:
$T=-\phi+(n b-m b)$ and $D=(-\phi(n b-m b))-(p \beta H / K)$. To obtain purely imaginary eigenvalues, we must have $T=0$ and $D>0$. But $T=0$ is only possible if $n b>m b$. But then $D<0$.

## Theorem (Bendixon's Criterion in $R^{n}$ )

A simple closed rectifiable curve which is invariant with respect to the differential equation, $\frac{d x}{d t}=f(x)$, cannot exist if any one of the following conditions is satisfied on $R^{n}$ :
(i) $\sup \left\{\frac{\partial f_{r}}{\partial x_{r}}+\frac{\partial f_{s}}{\partial x_{s}}+\sum_{q \neq r, s}\left(\left|\frac{\partial f_{q}}{\partial x_{r}}\right|+\left|\frac{\partial f_{q}}{\partial x_{s}}\right|\right): 1 \leq r<s \leq n\right\}<0$,
(ii) $\sup \left\{\frac{\partial f_{r}}{\partial x_{r}}+\frac{\partial f_{s}}{\partial x_{s}}+\sum_{q \neq r, s}\left(\left|\frac{\partial f_{r}}{\partial x_{q}}\right|+\left|\frac{\partial f_{s}}{\partial x_{q}}\right|\right): 1 \leq r<s \leq n\right\}<0$,
(iii) $\lambda_{1}+\lambda_{2}<0$,
iv) $\inf \left\{\frac{\partial f_{r}}{\partial x_{r}}+\frac{\partial f_{s}}{\partial x_{s}}+\sum_{q \neq r, s}\left(\left|\frac{\partial f_{q}}{\partial x_{r}}\right|+\left|\frac{\partial f_{q}}{\partial x_{s}}\right|\right): 1 \leq r<s \leq n\right\}>0$,
(v) $\sup \left\{\frac{\partial f_{r}}{\partial x_{r}}+\frac{\partial f_{s}}{\partial x_{s}}+\sum_{q \neq r, s}\left(\left|\frac{\partial f_{r}}{\partial x_{q}}\right|+\left|\frac{\partial f_{s}}{\partial x_{q}}\right|\right): 1 \leq r<s \leq n\right\}>0$,
(vi) $\lambda_{n-1}+\lambda_{n}>0$.
where the $\lambda_{i}$ are the ordered eigenvalues of $M=\frac{1}{2}\left[D f(x)+D f(x)^{T}\right]$.

## Periodic Solutions

$$
\begin{aligned}
\sup & \left\{-\mu-\beta\left(\frac{B}{K+B}\right)-\phi+p,-\phi+(n b-m b)+\frac{\beta S K}{(K+B)^{2}},-\mu+(n b-m b)+\frac{\beta S K}{(K+B)^{2}}\right\}<0 \\
p & \leq \mu+\beta\left(\frac{B}{K+B}\right)+\phi \\
p & \leq(n b-m b)+\frac{\beta S K}{(K+B)^{2}}+\mu+\beta\left(\frac{B}{K+B}\right) \\
p & <(n b-m b)+\frac{\beta S K}{(K+B)^{2}}+\phi+\beta\left(\frac{B}{K+B}\right) \\
\mu & \geq-n b+m b+-\frac{\beta S K}{(K+B)^{2}}-\frac{\beta B}{K+B}+p \\
\phi & \leq \mu \\
\phi & >n b-m b+\frac{\beta S K}{(K+B)^{2}} \\
\phi & \geq-n b+m b+-\frac{\beta S K}{(K+B)^{2}}-\frac{\beta B}{K+B}+p \\
\phi & \geq \mu \\
\phi & >n b-m b+\frac{\beta S K}{(K+B)^{2}}
\end{aligned}
$$

## The Networked Epidemic Model

First consider $n=3 \quad(i=1,2,3)$. This gives 9 differential equations:

$$
\begin{aligned}
\frac{d S_{i}}{d t} & =\mu\left(H_{i}-S_{i}\right)-\left[\left(1-m_{s}\right) \beta_{i} f\left(B_{i}\right)+m_{s} \sum_{j=1}^{n} Q_{i j} \beta_{j} f\left(B_{j}\right)\right] S_{i} \\
\frac{d l_{i}}{d t} & =\left[\left(1-m_{s}\right) \beta_{i} f\left(B_{i}\right)+m_{s} \sum_{j=1}^{n} Q_{i j} \beta_{j} f\left(B_{j}\right)\right] S_{i}-\phi I_{i} \\
\frac{d B_{i}}{d t} & =-\mu_{B} B_{i}+I\left(\sum_{j=1}^{n} P_{j i} \frac{W_{j}}{W_{i}} B_{j}-B_{i}\right)+\frac{p_{i}}{W_{i}}\left[\left(1-m_{l}\right) I_{i}+\sum_{j=1}^{n} m_{l} Q_{j i} I_{j}\right]
\end{aligned}
$$

## (Local) Stability Analysis of Three Communities

Jacobian $\mathbf{J}$ at disease-free equilibrium is
$\left[\begin{array}{ccccccccc}-\mu & 0 & 0 & 0 & 0 & 0 & -H_{1}\left(1-m_{S}\right) \beta_{1} & -H_{2} m_{S} Q_{12} \beta_{2} & -H_{3} m_{S} Q_{13} \beta_{3} \\ 0 & -\mu & 0 & 0 & 0 & 0 & -H_{1} m_{S} Q_{21} \beta_{1} & -H_{2}\left(1-m_{S}\right) \beta_{2} & -H_{3} m_{S} Q_{23} \beta_{3} \\ 0 & 0 & -\mu & 0 & 0 & 0 & -H_{1} m_{S} Q_{31} \beta_{1} & -H_{2} m_{S} Q_{32} \beta_{2} & -H_{3}\left(1-m_{S}\right) \beta_{3} \\ 0 & 0 & 0 & -\phi & 0 & 0 & H_{1}\left(1-m_{S}\right) \beta_{1} & H_{2} m_{S} Q_{12} \beta_{2} & H_{3} m_{S} Q_{13} \beta_{3} \\ 0 & 0 & 0 & 0 & -\phi & 0 & H_{1} m_{S} Q_{21} \beta_{1} & H_{2}\left(1-m_{S}\right) \beta_{2} & H_{3} m_{S} Q_{23} \beta_{3} \\ 0 & 0 & 0 & 0 & 0 & -\phi & H_{1} m_{S} Q_{31} \beta_{1} & H_{2} m_{S} Q_{32} \beta_{2} & H_{3}\left(1-m_{S}\right) \beta_{3} \\ 0 & 0 & 0 & \frac{p_{1}\left(1-m_{I}\right)}{W_{1} K} & \frac{p_{1} m_{I} Q_{21}}{W_{1} K} & \frac{p_{1} m_{I} Q_{31}}{W_{1} K} & -\mu_{B}-I & I P_{21} \frac{W_{2}}{W_{1}} & I P_{31} \frac{W_{3}}{W_{1}} \\ 0 & 0 & 0 & \frac{p_{2} m_{I} Q_{12}}{W_{2} K} & \frac{p_{2}\left(1-m_{I}\right)}{W_{2} K} & \frac{p_{2} m_{I} Q_{32}}{W_{2} K} & I P_{12} \frac{W_{1}}{W_{2}} & -\mu_{B}-I & I P_{32} \frac{W_{3}}{W_{2}} \\ 0 & 0 & 0 & \frac{p_{3} m_{I} Q_{13}}{W_{3} K} & \frac{p_{3} m_{I} Q_{23}}{W_{3} K} & \frac{p_{3}\left(1-m_{I}\right)}{W_{3} K} & I P_{13} \frac{W_{1}}{W_{3}} & I P_{23} \frac{W_{2}}{W_{3}} & -\mu_{B}-I\end{array}\right]$

Note: $B_{i}=B_{i} / K$

## (Local) Stability Analysis of Three Communities

We need to find general conditions for (local) stability.
We can block the Jacobian J as

$$
\begin{aligned}
& \mathbf{J}=\left[\begin{array}{ccc}
\mathbf{J}_{11} & 0 & \mathbf{J}_{13} \\
0 & \mathbf{J}_{22} & \mathbf{J}_{23} \\
0 & \mathbf{J}_{32} & \mathbf{J}_{33}
\end{array}\right] \quad \lambda(\mathbf{J})=\lambda\left(\mathbf{J}_{11}\right) \cup \lambda\left[\begin{array}{ll}
\mathbf{J}_{22} & \mathbf{J}_{23} \\
\mathbf{J}_{32} & \mathbf{J}_{33}
\end{array}\right] \\
& \mathbf{J}^{*}=\left[\begin{array}{ll}
\mathbf{J}_{22} & \mathbf{J}_{23} \\
\mathbf{J}_{32} & \mathbf{J}_{33}
\end{array}\right]
\end{aligned}
$$

Each block $\mathbf{J}_{i j}$ is a $3 \times 3$ matrix, and
$\mathbf{J}_{11}=\operatorname{diag}(-\mu)$.

## Irreducibility

## Definition

A matrix $A_{n \times n}$ is reducible if it is similar to a block triangular matrix: There is a permutation matrix P such that

$$
P^{T} A P=\left[\begin{array}{ll}
B & C \\
0 & D
\end{array}\right], 0 \in \mathbf{R}^{r \times(n-r)},(1 \leq r \leq n-1)
$$

A matrix is irreducible if it is not reducible.

## (Local) Stability Analysis of Three Communities

$\mathbf{J}^{*}$ is given by
$\left[\begin{array}{cccccc}-\phi & 0 & 0 & H_{1}\left(1-m_{S}\right) \beta_{1} & H_{2} m_{S} Q_{12} \beta_{2} & H_{3} m_{S} Q_{13} \beta_{3} \\ 0 & -\phi & 0 & H_{1} m_{S} Q_{21} \beta_{1} & H_{2}\left(1-m_{S}\right) \beta_{2} & H_{3} m_{S} Q_{23} \beta_{3} \\ 0 & 0 & -\phi & H_{1} m_{S} Q_{31} \beta_{1} & H_{2} m_{S} Q_{32} \beta_{2} & H_{3}\left(1-m_{S}\right) \beta_{3} \\ \frac{p_{1}\left(1-m_{l}\right)}{W_{1} K} & \frac{p_{1} m_{l} Q_{21}}{W_{1} K} & \frac{p_{1} m_{l} Q_{31}}{W_{1} K} & -\mu_{B}-I & I P_{21} \frac{W_{2}}{W_{1}} & I P_{31} \frac{W_{3}}{W_{1}} \\ \frac{p_{2} m_{l} Q_{12}}{W_{2} K} & \frac{p_{2}\left(1-m_{l}\right)}{W_{2} K} & \frac{p_{2} m_{l} Q_{32}}{W_{2} K} & I P_{12} \frac{W_{1}}{W_{2}} & -\mu_{B}-I & I P_{32} \frac{W_{3}}{W_{2}} \\ \frac{p_{3} m_{l} Q_{13}}{W_{3} K} & \frac{p_{3} m_{l} Q_{23}}{W_{3} K} & \frac{p_{3}\left(1-m_{I}\right)}{W_{3} K} & I P_{13} \frac{W_{1}}{W_{3}} & I P_{23} \frac{W_{2}}{W_{3}} & -\mu_{B}-I\end{array}\right]$

J* is irreducible.

## Metzler Matrix

## Definition

A matrix $\mathbf{M}$ is said to be Metzler if all of the off-diagonal entries are nonnegative.
(1) If you have an $\mathbf{M}_{n x n}$ Metzler matrix, then the eigenvalue with maximum real part is real.

$$
\alpha(\mathbf{M})=\max _{i} \operatorname{Re} \lambda_{i}(\mathbf{M}), \quad i=1,2, \ldots, n
$$

(2) The Metzler matrix, $\mathbf{M}$, is asymptotically stable iff $\alpha(\mathbf{M})<0$

$$
\text { Therefore } \mathbf{J}^{*} \text { is a Metzler matrix. }
$$

## (Local) Stability Analysis of Three Communities

A very useful variation of Perron-Frobenius theorem:

## Theorem

Let $\mathbf{M} \in \mathbb{R}^{n \times n}$ be a Metzler matrix. If $\mathbf{M}$ is irreducible, then $\lambda^{*}=\alpha(M)$ is a simple eigenvalue, and its associated eigenvector is positive.

When $\lambda^{*}$ reaches zero, the $\operatorname{det}\left(\mathbf{J}^{*}\right)=0$ and the disease free equilibrium point will lose stability.

$$
\mathbf{J}^{*}=\left[\begin{array}{ll}
\mathbf{J}_{22} & \mathbf{J}_{23} \\
\mathbf{J}_{32} & \mathbf{J}_{33}
\end{array}\right], \quad \operatorname{det}\left(\mathbf{J}^{*}\right)=\left(\mathbf{J}_{22} \mathbf{J}_{33}\right)-\left(\mathbf{J}_{23} \mathbf{J}_{32}\right)=0
$$

$$
\begin{aligned}
& \mathbf{J}_{22}=-\phi \mathbf{U}_{\mathbf{3}} \\
& \mathbf{J}_{23}=m_{S} \mathbf{H} \mathbf{Q} \boldsymbol{\beta}+\left(1-m_{S}\right) \mathbf{H} \boldsymbol{\beta} \\
& \mathbf{J}_{23}= \frac{m_{I}}{K} \mathbf{p} \mathbf{W}^{-1} \mathbf{Q}^{\boldsymbol{\top}}+ \\
& \mathbf{J}_{33}= \frac{1-m_{I}}{K} \mathbf{p} \mathbf{W}^{-1} \\
& \operatorname{det}\left(\mu_{B}+I\right) \mathbf{U}_{\mathbf{3}}+ I \mathbf{W}^{-1} \mathbf{P}^{\top} \mathbf{W} \\
&= \operatorname{det}\left[\phi\left(\mu_{B}+I\right) \mathbf{U}_{\mathbf{3}}-\phi / \mathbf{W}^{-1} \mathbf{P}^{\top} \mathbf{W}-\frac{m_{S} m_{l}}{K} \mathbf{p} \mathbf{W}^{-1} \mathbf{Q}^{T} \mathbf{H} \mathbf{Q} \boldsymbol{\beta}\right. \\
&-\frac{m_{l}\left(1-m_{S}\right)}{K} \mathbf{p} \mathbf{W}^{-1} \mathbf{Q}^{\top} \mathbf{H} \boldsymbol{\beta}-\frac{\left(1-m_{l}\right) m_{S}}{K} \mathbf{p} \mathbf{W}^{-1} \mathbf{H} \mathbf{Q} \boldsymbol{\beta} \\
&\left.-\frac{\left(1-m_{I}\right)\left(1-m_{S}\right)}{K} \mathbf{p} \mathbf{W}^{-1} \mathbf{H} \boldsymbol{\beta}\right]=0
\end{aligned}
$$

where $\mathbf{p}, \mathbf{H}, \boldsymbol{\beta}, \mathbf{W}, \mathbf{W}^{-1}$ are diagonal, hence commute with each other.

## Determinant of J*

One can prove that $\operatorname{det}\left(\mathbf{J}^{*}\right)=0 \Longleftrightarrow \operatorname{det}\left(\mathbf{U}_{\mathbf{3}}-\mathbf{G}_{\mathbf{0}}\right)=0$
Thus, the the disease-free equilibrium loses stability when $\operatorname{det}\left(\mathbf{U}_{\mathbf{3}}-\mathbf{G}_{\mathbf{0}}\right)=0$, where

$$
\mathbf{G}_{0}=\frac{l}{\mu_{B}+l} \mathbf{P}^{T}+\frac{\mu_{B}}{\mu_{B}+l} \mathbf{T}_{\mathbf{0}}
$$

$\mathrm{T}_{0}=$
$\left(1-m_{l}\right)\left(1-m_{S}\right) \mathbf{R}_{\mathbf{0}}+m_{S} m_{l} \mathbf{R}_{\mathbf{0}}^{\mathbf{I S}}+m_{l}\left(1-m_{S}\right) \mathbf{R}_{\mathbf{0}}^{\mathbf{I}}+\left(1-m_{l}\right) m_{S} \mathbf{R}_{\mathbf{0}}^{\mathbf{S}}$.

Is a transcritical bifurcation happening here?
Stay put!

## Theorems

## Theorem (Perron-Frobenius)

If $A_{n \times n}$ is non-negative and irreducible, then:
(1) $\rho(A)$ is a positive eigenvalue of $A$
(2) The eigenvector associated to $\rho(A)$ is positive
(3) The algebraic and geometric multiplicity of $\rho(A)$ is 1

## Theorem (Berman, Plemmons)

Let $A=s l-B$, where $B$ is an nxn nonnegative matrix. If there exists a vector $x>0$, such that $A x \geq 0$, then $\rho(B) \leq s$.

## Dominant Eigenvalue

- $\mathbf{G}_{0}>0$ and irreducible
- $\rho\left(\mathbf{G}_{\mathbf{0}}\right)$ is a simple eigenvalue (Perron-Frobenius)
- $\operatorname{det}\left(\mathbf{U}_{\mathbf{3}}-\mathbf{G}_{\mathbf{0}}\right)=0$ implies 1 is an eigenvalue of $\mathbf{G}_{\mathbf{0}}$
- $\rho\left(\mathbf{G}_{0}\right) \leq 1$ (Berman, Plemmons)

Therefore, $\rho\left(\mathbf{G}_{0}\right)=1$ and 1 is the dominant eigenvalue.
This proves: The disease free equilibrium loses stability when $\rho\left(\mathbf{G}_{\mathbf{0}}\right)$ crosses one, and an outbreak occurs.
$\rho\left(\mathbf{G}_{\mathbf{0}}\right)$ is called the Generalized Reproduction Number.

## Lyapunov Functions and Global Asymptotic Stability

First write equations as a compartmental system:
$\mathbf{x}^{\prime}=\mathbf{F}^{*}(x, y)-\mathbf{V}^{*}(x, y), \quad \mathbf{y}^{\prime}=g(x, y)$
where $\mathbf{x}=\left[\begin{array}{lllll}l_{1} & l_{2} & l_{3} & B_{1} & B_{2}\end{array} B_{3}\right]^{\top}$ and $\mathbf{y}=\left[\begin{array}{lll}S_{1} & S_{2} & S_{3}\end{array}\right]^{\top}$.

- $R_{0} \leq 1$ does not determine stability for connected communities.
- Cannot use $\rho\left(\mathbf{G}_{\mathbf{0}}\right)$
- Need to find a new condition.
- Exploited the fact that $\mathbf{J}^{*}=\mathbf{F}-\mathbf{V}$ to prove:

$$
\lambda^{*}\left(\mathbf{J}^{*}\right) \leq 0 \quad \Leftrightarrow \quad \tilde{\lambda}^{*}\left(\mathbf{V}^{-1} \mathbf{J}^{*}\right) \leq 0 \quad \Leftrightarrow \quad \lambda_{F}^{*}\left(\mathbf{V}^{-1} \mathbf{F}\right) \leq 1
$$

The three matrices above are Metzler!

## Lyapunov Functions and Global Asymptotic Stability

## Theorem

Let $0<\lambda_{F}^{*}\left(\mathbf{V}^{-1} \mathbf{F}\right) \leq 1$, and let $\mathbf{w}$ be a left eigenvector of $\mathbf{V}^{-1} \mathbf{F}$ corresponding to $\lambda_{F}^{*}\left(\mathbf{V}^{-1} \mathbf{F}\right)$. Then the function $Q(\mathbf{x})=\mathbf{w}^{T} \mathbf{V}^{-1} \mathbf{x}$ is a Lyapunov function satisfying $Q^{\prime} \leq 0$.

$$
\begin{aligned}
Q= & \frac{1}{K \phi\left(\mu_{B}+l\right) \lambda_{F}^{*}}\left[I_{1}\left(\frac{p_{1}\left(1-m_{I}\right)}{W_{1}}+\frac{p_{2} m_{l} Q_{12}}{W_{2}}+\frac{p_{3} m_{I} Q_{13}}{W_{3}}\right)+\right. \\
& +I_{2}\left(\frac{p_{1} m_{l} Q_{21}}{W_{1}}+\frac{p_{2}\left(1-m_{I}\right.}{W_{2}}+\frac{p_{3} m_{l} Q_{23}}{W_{3}}\right)+ \\
& \left.+I_{3}\left(\frac{p_{1} m_{I} Q_{31}}{W_{1}}+\frac{p_{2} m_{I} Q_{32}}{W_{2}}+\frac{p_{3}\left(1-m_{I}\right)}{W_{3}}\right)\right]+ \\
& +\frac{1}{\mu_{B}+l}\left(B_{1}+B_{2}+B_{3}\right)
\end{aligned}
$$

$Q\left(\mathbf{x}_{0}\right)=Q(\mathbf{0}, \mathbf{0}, \mathbf{H})=0$ and $Q(\mathbf{x})>0$ when $\mathbf{x} \neq \mathbf{x}_{0}$.
$Q^{\prime}=\left(\lambda_{F}^{*}-1\right) \mathbf{w}^{T} \mathbf{x}-\mathbf{w}^{T} \mathbf{V}^{-1} \mathbf{f}(x, y) \leq 0$

## Lyapunov Functions and Global Asymptotic Stability

## Theorem (LaSalle's Invariance Principle)

Let $\Omega \subset D \subset R^{n}$ be a compact invariant set with respect to $x^{\prime}=f(x)$. Let $Q: D \rightarrow R$ be a $C^{1}$ function such that $Q^{\prime}(x(t)) \leq 0$ in $\Omega$. Let $E \subset \Omega$ be the set of all points in $\Omega$ where $Q^{\prime}(x)=0$. Let $M \subset E$ be the largest invariant set in $E$. Then

$$
\lim _{t \rightarrow \infty}\left[\inf _{y \in M}\|x(t)-y\|\right]=0
$$

That is, every solution starting in $\Omega$ approaches $M$ as $t \rightarrow \infty$.

## Lyapunov Functions and Global Asymptotic Stability

Using LaSalle's invariance principle we can now prove global asymptotic stability.

## Theorem

Let $\Omega$ be any compact invariant set containing the disease-free equilibrium point of the compartmental model and let $\mathbf{F}, \mathbf{V}$, $\mathbf{V}^{-1} \geq 0, \mathbf{f}(x, y) \geq 0$, and $\mathbf{f}(0, y)=0$. Assume $0<\lambda_{F}^{*}\left(\mathbf{V}^{-1} \mathbf{F}\right)<1$ and assume the disease-free system $\mathbf{y}^{\prime}=g(0, y)$ has a unique equilibrium $\mathbf{y}=\mathbf{y}_{0}>0$ that is globally asymptotically stable in the disease-free system. Then, the disease-free equilibrium of the nine-dimensional system is globally asymptotically stable in $\Omega$.

## Lyapunov Functions and Global Asymptotic Stability

Solving for $\boldsymbol{S}$ explicitly gives $\mathbf{S}=\left[\begin{array}{l}H_{1}+e^{-\mu t} C_{1} \\ H_{2}+e^{-\mu t} C_{2} \\ H_{3}+e^{-\mu t} C_{3}\end{array}\right]$.
$Q^{\prime}=\left(\lambda_{F}^{*}-1\right) \mathbf{w}^{T} \mathbf{x}-\mathbf{w}^{T} \mathbf{V}^{-1} \mathbf{f}(x, y)$. Assuming $Q^{\prime}=0$ implies $\mathbf{x}=0$. Then, the set of all points where $Q^{\prime}=0$ is
$E=\left\{\left(I_{i}, B_{i}, S_{i}\right): I_{i}=B_{i}=0\right\}$.
Applying LaSalle's invariance principle shows that the disease-free equilibrium is globally asymptotically stable.

## Existence of Endemic Equilibrium

Recall that $\lambda^{*}\left(\mathbf{J}^{*}\right) \leq 0 \quad \Longleftrightarrow \quad \lambda_{F}^{*}\left(\mathbf{V}^{-1} \mathbf{F}\right) \leq 1$.

## Theorem

Let $\Omega$ be any compact invariant set containing the disease-free equilibrium point of compartmental model. Let $\mathbf{F}, \mathbf{V}, \mathbf{V}^{-1} \geq 0$, $\mathbf{f}(x, y) \geq 0$, and $\mathbf{f}(0, y)=0$. If $\lambda^{*}\left(\mathbf{J}^{*}\right)>0$, then there exists at least one endemic equilibrium.

## Hydrological Transportation and Human Mobility

$$
P_{i j}=\left\{\begin{array}{cl}
\frac{P_{\text {out }}}{d_{\text {out }}(i) P_{\text {out }}+d_{\text {in }}(i) P_{\text {in }}} & \text { if } i \rightarrow j \\
\frac{P_{\text {in }}}{d_{\text {out }}(i) P_{\text {out }}+d_{\text {in }}(i) P_{\text {in }}} & \text { if } i \leftarrow j \\
0 & \text { otherwise }
\end{array}\right.
$$

$$
Q_{i j}=\frac{H_{j} e^{\left(-d_{i j} / D\right)}}{\sum_{k \neq i}^{n} H_{k} e^{\left(-d_{i k} / D\right)}}
$$

## Geography of Disease Onset

$$
\begin{gathered}
\mathbf{J}^{*}\left[\begin{array}{l}
\mathbf{i} \\
\mathbf{b}
\end{array}\right]=\lambda^{*}\left[\begin{array}{l}
\mathbf{i} \\
\mathbf{b}
\end{array}\right] \\
\mathbf{J}^{*}=\left[\begin{array}{ll}
\mathbf{A} & \mathbf{B} \\
\mathbf{C} & \mathbf{D}
\end{array}\right]
\end{gathered}
$$

$\mathbf{A i}+\mathbf{B b}=\lambda^{*} \mathbf{i}$
$\mathbf{C i}+\mathbf{D b}=\lambda^{*} \mathbf{b}$
$\mathbf{i}=-\mathbf{A}^{-1} \mathbf{B b}$ and we can re-write the above expression as
$\mathbf{C A}^{-1} \mathbf{B b}+\mathbf{D d}=0$
$(\mathbf{A D}-\mathbf{C B}) \mathbf{b}=0$

## Geography of Disease Onset

After MUCH simplification, we get

$$
\mathbf{A D}-\mathbf{C B}=\phi\left(\mu_{B}+I\right)\left[\mathbf{U}_{\mathbf{3}}-\mathbf{W}^{-1}\left(\frac{l}{\mu_{B}+l} \mathbf{P}^{T}+\frac{\mu_{B}}{\mu_{B}+l} \mathbf{T}_{\mathbf{0}}\right) \mathbf{W}\right]
$$

Substituting $\mathbf{G}_{\mathbf{0}}$, we get

$$
\mathbf{A D}-\mathbf{C B}=\phi\left(\mu_{B}+I\right)\left(\mathbf{U}_{\mathbf{3}}-\mathbf{W}^{-1} \mathbf{G}_{\mathbf{0}} \mathbf{W}\right)
$$

We can now write $\left(\mathbf{U}_{\mathbf{3}}-\mathbf{W}^{-\mathbf{1}} \mathbf{G}_{\mathbf{0}} \mathbf{W}\right) \mathbf{b}=0$, then

$$
\mathbf{W b}=\mathbf{G}_{0} \mathbf{W} \mathbf{b}
$$

Thus, $\mathbf{W b}$ is the eigenvector of $\mathbf{G}_{\mathbf{0}}$ associated to the eigenvalue $\lambda=1$.

## Geography of Disease Onset

$$
\mathbf{i}=\mathbf{A}^{-1} \mathbf{B b}
$$

After substitution and simplification we get,

$$
\mathbf{i}=\frac{m_{s} \mathbf{H} \mathbf{Q} \boldsymbol{\beta}+\left(1-m_{s}\right) \mathbf{H} \boldsymbol{\beta}}{\phi}\left(\mathbf{W}^{-1} \mathbf{g}_{0}\right)
$$

## Bifurcations

- Recall that $\mathbf{J}^{*}$ determines stability of disease-free equilibrium, and is a Metzler matrix.
- When $\lambda^{*}=0$ stability is lost.
- Proved existence of transcritical bifurcation using Sotomayor's theorem.
- Choose $p_{1}$ to be our varying parameter.


## Sotomayor's Theorem

Let $\mathbf{f}=\left[\begin{array}{llll}f_{1} & f_{2} & \cdots & f_{9}\end{array}\right]^{T}$, and $\mathbf{x}=\left(\begin{array}{llllllll}S_{1} & S_{2} & S_{3} & I_{1} & I_{2} & I_{3} & B_{1} & B_{2}\end{array} B_{3}\right)^{T}$ so $\mathbf{x}_{0}=\left(H_{1} H_{2} H_{3} 00000000\right)^{T}$.

Take partial derivatives of $\mathbf{f}$ with respect to $p_{1}$ to arrive at the vector

$$
\mathbf{f}_{p_{1}}=\left[\begin{array}{c}
0 \\
0 \\
0 \\
0 \\
0 \\
0 \\
{\left[\left(1-m_{l}\right) l_{1}+m_{l}\left(Q_{21} l_{2}+Q_{31} l_{3}\right)\right] W_{1}^{-1}} \\
0 \\
0
\end{array}\right]
$$

First condition : $\mathbf{w}^{T} \mathbf{f}_{p_{1}}\left(\mathbf{x}_{0}, p_{1}^{0}\right)=0$

## Sotomayor's Theorem

Second condition:

$$
\begin{aligned}
& \mathbf{w}^{T}\left[D \mathbf{f}_{p_{1}}\left(\mathbf{x}_{0}, p_{1}^{0}\right) \mathbf{v}\right]= \\
& \frac{H_{1}}{\phi}\left[\left(1-m_{S}\right) \beta_{1}+m_{S} Q_{12} \beta_{2}+m_{S} Q_{13} \beta_{3}\right]\left(1-m_{l}\right) W_{1}^{-1}+ \\
& \frac{H_{2}}{\phi}\left[m_{S} Q_{21} \beta_{1}+\left(1-m_{S}\right) \beta_{2}+m_{S} Q_{23} \beta_{3}\right] m_{l} Q_{21} W_{1}^{-1}+ \\
& \frac{H_{3}}{\phi}\left[m_{S} Q_{31} \beta_{1}+m_{S} Q_{32} \beta_{2}+\left(1-m_{S}\right) \beta_{3}\right] m_{l} Q_{31} W_{1}^{-1} \neq 0
\end{aligned}
$$

## Sotomayor's Theorem

$D^{2} \mathbf{f}\left(\mathbf{x}_{0}, p_{1}^{0}\right)(\mathbf{v}, \mathbf{v})$ is found.
Third condition: $\mathbf{w}^{T}\left[D^{2} \mathbf{f}\left(\mathbf{x}_{0}, p_{1}^{0}\right)(\mathbf{v}, \mathbf{v})\right]=$ $w_{4}\left(2\left(1-m_{S}\right) \beta_{1} v_{1}+2 m_{S} Q_{12} \beta_{2} v_{1}+2 m_{S} Q_{13} \beta_{3} v_{1}\right.$
$\left.-2 H_{1}\left(1-m_{S}\right) \beta_{1}-2 H_{1} m_{S} Q_{12} \beta_{2}-2 H_{1} m_{S} Q_{13} \beta_{3}\right)$
$+w_{5}\left(2 m_{S} Q_{21} \beta_{1} v_{2}+2\left(1-m_{S}\right) \beta_{2} v_{2}+2 m_{S} Q_{23} \beta_{3} v_{2}\right.$
$\left.-2 H_{2} m_{S} Q_{21} \beta_{1}-2 H_{2}\left(1-m_{S}\right) \beta_{2}-2 H_{2} m_{S} Q_{23} \beta_{3}\right)$
$+w_{6}\left(2 m_{S} Q_{31} \beta_{1} v_{3}+2 m_{S} Q_{32} \beta_{2} v_{3}+2\left(1-m_{S}\right) \beta_{3}\right.$
$\left.-2 H_{3} m_{S} Q_{31} \beta_{1}-2 H_{3} m_{S} Q_{32} \beta_{2}-2 H_{3}\left(1-m_{S}\right) \beta_{3}\right) \neq 0$

## $\mathbf{p}<\mathbf{p}_{0}$

DFE $=(10000,13000,11000,0,0,0,0,0,0)$


## $\mathbf{p}=\mathbf{P}_{0}$



## p > $\mathbf{p}_{0}$

$$
\mathrm{EE}=(11.195,14.708,12.952,215.439,280.068,236.969,0.135,0.097,0.157)
$$



## $n$ Number of Communities

The Jacobian at the disease-free equilibrium $x_{0}=\left(H_{1}, H_{2}, \ldots, H_{n}, 0, \ldots, 0\right)$ is given by

$$
\mathbf{J}\left(\mathbf{x}_{0}\right)=\left[\begin{array}{ccc}
\mathbf{J}_{11} & 0 & \mathbf{J}_{13} \\
0 & \mathbf{J}_{22} & \mathbf{J}_{23} \\
0 & \mathbf{J}_{32} & \mathbf{J}_{33}
\end{array}\right]
$$

where each $\mathbf{J}_{i j}$ block is an $n \times n$ matrix, and
$\mathbf{J}_{11}=-\mu \mathbf{U}_{\mathbf{n}}$
$\mathbf{J}_{13}=-m_{S} \mathbf{H} \mathbf{Q} \boldsymbol{\beta}-\left(1-m_{S}\right) \mathbf{H} \boldsymbol{\beta}$
$\mathbf{J}_{22}=-\phi \mathbf{U}_{\mathbf{n}}$
$\mathbf{J}_{23}=m_{s} \mathbf{H Q} \boldsymbol{\beta}+\left(1-m_{s}\right) \mathbf{H} \boldsymbol{\beta}$
$\mathrm{J}_{32}=\frac{m_{\mathbf{l}}}{K} \mathbf{p W}^{-1} \mathbf{Q}^{\boldsymbol{\top}}+\frac{1-m_{l}}{K} \mathbf{p W}^{-1}$
$\mathbf{J}_{33}=-\left(\mu_{\boldsymbol{B}}+I\right) \mathbf{U}_{\mathbf{n}}+I \mathbf{W}^{-\mathbf{1}} \mathbf{P}^{\boldsymbol{\top}} \mathbf{W}$

## Math Commandments

(1) The disease-free equilibrium loses stability when $\lambda^{*}\left(\mathbf{J}^{*}\right)$ crosses zero.
(2) The system undergoes a transcritical bifurcation when $\lambda^{*}\left(\mathbf{J}^{*}\right)$ crosses zero.
(3) The condition $\operatorname{det}\left(\mathbf{J}^{*}\right)=0$ is equivalent to $\operatorname{det}\left(\mathbf{U}_{\mathbf{n}}-\mathbf{G}_{\mathbf{0}}\right)=0$.
(4) $\lambda=1$ is the dominant eigenvalue of $\mathbf{G}_{0}$.
(5) If $0<\lambda_{F}^{*}\left(\mathbf{V}^{-1} \mathbf{F}\right) \leq 1$, then $Q=\mathbf{w}^{\top} \mathbf{V}^{-1} \mathbf{x}$ is a Lyapunov function satisfying $Q^{\prime} \leq 0$.
(6) If $0<\lambda_{F}^{*}\left(\mathbf{V}^{-1} \mathbf{F}\right)<1$ and the disease-free equilibrium is globally asymptotically stable in the disease-free system, then it is a globally asymptotically stable equilibrium of the general system.

## Math Commandments Cont.

(7) If $\lambda^{*}\left(\mathbf{J}^{*}\right)>0$, then the system has at least one endemic equilibrium point.

8 The dominant eigenvector of $\mathbf{G}_{\mathbf{0}}$, once projected onto the subspace of infectives, provides us with an effective way to forecast the geographical spread of the disease.
(9) Under some conditions, no periodic orbits can exist ( $\mathrm{n}=1$ ).
(10) The system has no Hopf bifurcations at DFE $(\mathrm{n}=1)$.

## Our Contribution

- $n=1$
- Found correct endemic equilibrium point
- Proved global stability of DFE
- Proved existence of transcritical bifurcation
- (Non)existence of periodic solutions
- $n>1$ (Networked Connectivity Model)
- Established a new condition for outbreak of epidemics
- Introduced an appropriate Lyapunov function
- Proved global stability of DFE
- Proved existence of transcritical bifurcation
- Proved existence of endemic equilibrium
- Numerical evidence of homoclinic orbit


## Back to the Future:

- Proving the existence of the homoclinic orbit.
- Conditions for global stability of endemic equilibrium.
- Hopf bifurcation at endemic equilibrium.
- Get help from XPPAUT to find some other possible bifurcations.
- Include seasonal behavior of some diseases.
- Include water treatment/sanitation and vaccination in the model
- Lunch at Union Club: Chicken Parmesan
- Come back to MSU for MAKO conference!!!!

Introduction
$n=1$
$n=3$
General n What's Next 00000000


